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A comparative analysis of supply chain factors impacting COVID-19 vaccine security in high-income countries (HICs) and low-income and middle-income countries (LMICs)

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ABSTRACT

Introduction The COVID-19 pandemic focused attention on the importance of vaccine security to national security. Demand for vaccines far exceeded supply when the first COVID-19 vaccines were released. Growing data suggest a non-perfect correlation among vaccine development, production, purchases, deliveries and vaccination rates. As such, the best approach to strengthening vaccine security remains unclear. In this study, we use an operations research/operations management framework to characterise the relationship between vaccine security and key supply chain predictor variables in high-income countries (HICs) and low-income and middle-income countries (LMICs).

Methods We performed a comparative analysis of vaccine security against eight supply chain variables in a purposive sample of five HICs and five LMICs during the early phase of the pandemic (31 March 2021 and 30 April 2021). All data were obtained from publicly available databases. We used descriptive statistics to characterise our data, basic statistics to compare data and scatter plots to visualise relationships.

Results Our data show greater vaccine security in HICs compared with LMICs (32.2% difference in April 2021; 95% CI 4.2% to 60.3%, p=0.03). We report a significant difference between HICs and LMICs in only two of the eight predictor variables studied. Interestingly, we observed large variation in vaccine security *within* HICs, with Canada, Israel and Japan being frequent outliers, and within LMICs, with India standing out.

Conclusion Our data suggest a stronger relationship between vaccine security and 'downstream' supply chain variables compared with 'upstream' variables. However, multiple outliers and the lack of an even stronger relationship suggests that there is no magic bullet for vaccine security. To boost vaccine resilience, countries must be well governed and strategically reinforce deficient aspects of their supply chains. Modest strength in multiple domains may be the best approach to counteracting the effect of an unfamiliar, novel pathogen.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Even prior to the COVID-19 pandemic, the vaccine supply chain literature emphasised the importance of taking an integrated supply chain view and warned that improving any single aspect of vaccine logistics without alignment with other components was unlikely to lead to overall improvement. We are unaware of any published studies after the COVID-19 pandemic that examine vaccine security among high-income countries and low-income and middle-income countries through an operations research/operations management framework.

WHAT THIS STUDY ADDS

⇒ When faced with the unanticipated threats posed by a novel pandemic such as COVID-19, the optimal approach to vaccine security remains unclear. Our study suggests that countries may achieve greater vaccine security by modestly strengthening multiple deficient aspects of their supply chains, rather than relying on only one or a few aspects of preparedness.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ As there does not appear to be any silver bullet for vaccine security, nations must develop global and regional frameworks that create resilience in all four phases of the vaccine supply chain. Our lessons may help key stakeholders to maximise the health security of their people during future pandemics.

INTRODUCTION

According to the WHO, vaccine security is the timely, sustained and uninterrupted supply of affordable vaccines of assured quality.[1] In April 2020, at the outset of the COVID-19 pandemic, WHO established the Access to COVID-19 Tools Accelerator which included COVAX, an organisation whose goal was to accelerate the development and manufacture of COVID-19 vaccines, while guaranteeing fair and equitable access for every country in the world.[2]

As the first COVID-19 vaccines came onto the market in late 2020, demand vastly outstripped supply and we saw the rise of what has been labelled 'vaccine nationalism'.[3] Even before any vaccine candidates were approved, many high-income countries (HICs) hedged their bets and signed bilateral purchase deals with manufacturers to vaccinate their populations several times over, leaving a smaller piece of the pie for low-income and middle-income countries (LMICs) and equity-focused partnerships such as COVAX. While the media have framed vaccine security as a binary between HICs and LMICs, there are growing data to suggest that vaccine purchases, vaccine deliveries and vaccination rates did not perfectly correlate, even among HICs.[4]

Prior to the COVID-19 pandemic, there was already a growing interest in the operations research/operations management (OR/OM) literature on vaccine supply chains. In a 2018 review, Duijzer *et al* proposed a vaccine supply chain framework comprised of four elements: (1) product, (2) production, (3) allocation and (4) distribution.[5] In 2014, Privett and Gonsalvez emphasised the importance of taking an integrated view over a whole supply chain and warned that improving any single aspect of vaccine logistics without alignment with other components was only likely to lead to minor overall improvements.[6] As vaccine availability is dynamic over the medium term, insights from game theory analysis suggest that vaccine security is not a 'zero sum game' and that even bilateral deals between a nation and a vaccine maker can be configured in ways to enhance supply chain harmonisation.[7]

In 1978, Tanahashi characterised the challenges that health systems face when expanding healthcare coverage.[8] In stepwise fashion, the rate-limiting variables are: availability, accessibility, acceptability, contact and effectiveness. By applying the Tanahashi framework, it is evident that vaccine availability was the main rate-limiting step globally in the immediate phase post COVID-19 vaccine emergency use authorisation in late 2020/early 2021.

We are unaware of any published studies that examine vaccine security among HICs and LMICs through an OR/OM framework. Taking a supply chain perspective, we hypothesise that there were differences in vaccine security in late March and April 2021 among countries that may be explained by predictor variables at all four stages of the supply chain framework, namely (1) product (novel vaccine development capability), (2) production (domestic vaccine manufacturing capacity), (3) allocation (ability to secure advance market commitment (AMC) purchases from vaccine manufacturers) and (4) distribution (vaccine deliveries from manufacturer to purchaser).[9]

Our study has three objectives. First, to describe vaccine security in HICs and LMICs, and quantify the difference between these groupings. Second, to characterise the relationship between vaccine security and key supply chain predictor variables in HICs and LMICs. Third, to draw lessons from the COVID-19 experience in HICs and LMICs to assist key stakeholders with optimising vaccine security during future pandemics.

METHODS

Study countries

Using the four-stage vaccine supply chain framework proposed by Duijzer *et al*,[5] we sought to perform a comparative analysis of supply chain factors in a purposive sample of five HICs, namely USA, Israel, Canada, UK, Japan and five LMICs, namely Brazil, Peru, Vietnam, India and Guinea. Our sample was chosen after a knowledge synthesis to account for (1) heterogeneity in predictor supply chain variable capabilities, (2) geographical variety and (3) adequacy of publicly available critical data elements. Where needed, the LMICs were further subcategorised into upper middle-income countries (UMICs), that is, Brazil and Peru, lower middle-income countries, that is, Vietnam and India, and low-income countries, that is, Guinea. We used 2021 World Bank country classifications by income level that are based on gross national income (GNI) per capita in current US dollars (USD).[10]

Data collection

All data for this study were obtained from the following major publicly available databases: Our World In Data,[11] COVID-19 Vaccine Tracker,[12] COVID-19 Market Dashboard,[13] World Bank's World Integrated Trade Solution (WITS) software,[14] Launch and Scale Speedometer,[15] Duke Global Health Innovation Center[16] and World Bank Total Population Statistics.[17] These databases had comprehensive data at multiple timepoints for all the measures described below except COVID-19-specific vaccine production capacity. Raw data was downloaded from these databases by one author (MP) and corroborated by the remaining authors. Specific search terms used for each data extraction and data analysis methods are described in detail in the sections below. As there were no publicly available databases with comprehensive data on COVID-19 vaccine production capacity at multiple timepoints, we obtained data from Statista[18] and Global Commission for Post-Pandemic Policy[19] reports.

Measures

Data for national vaccination rates was from Our World In Data using their 'Data explorer' with the metric 'People vaccinated' and the interval 'Cumulative'.[11] For this study, the percentage of a country's population that received one dose of any COVID-19 vaccine at or before two timepoints, 31 March 2021 and 30 April 2021, was taken as a proxy for vaccine security. These timepoints were chosen after an analysis of national vaccination rates in the 6 months post emergency use authorisation (December 2020 to May 2021) revealed wide variation between the countries in our sample.[11 12] We focused on earlier timepoints as vaccine availability was more likely to be the main health systems bottleneck to vaccine security, prior to downstream Tanahashi factors, such as accessibility and acceptability becoming barriers to vaccine security. As our study focused on the 'high demand and low supply' early phase of the pandemic described by Bongers *et al*,[20] our observations are most applicable to 'initial vaccine security', and may not be extrapolated to the later 'low demand, high supply' phase of the pandemic when factors such as hesitancy significantly impacted vaccine security.

To determine the best supply chain predictor variables, we studied two factors at each of the four stages of the vaccine supply chain. To characterise the product stage, that is, the ability of countries to develop a novel COVID-19 vaccine, we first retrospectively examined the number of COVID-19 vaccine makers in each country as of June 2023. Data was derived from the COVID-19 Market Dashboard using the tabs 'Vaccines', 'Products' and 'By developer country'.[13] Both vaccine products 'approved for use' and at 'all development stages' were compared. Given heterogeneity in vaccine platforms and the emergence of new vaccine development partnerships during the pandemic, we postulated that countries with a greater number of vaccine makers in June 2023 would have had a more robust domestic vaccine development programme at the outset of the pandemic. Next, we examined global vaccine trade data from the World Bank's WITS software prospectively to determine if countries were net importers or exporters of vaccines in 2019, just prior to the pandemic.[14] We theorised that net vaccine exporters would possess greater 'know-how' prior to the pandemic and have increased vaccine development capacity.

Given limited public data on vaccine production capacity, we assessed COVID-19 vaccine specific manufacturing capacity by comparing the number of COVID-19 vaccine doses produced in each country as of 3 March 2021. Data was from Statista[18] and the Global Commission for Post-Pandemic Policy.[19] To our knowledge, there are no public sources with this data as of 31 March and 30 April 2021. In addition, we compared the number of unique COVID-19 vaccine manufacturing facilities (any stage of production) in each country as of 30 June 2022 from the Launch and Scale Speedometer using the tab 'All vaccines'.[15] This was corroborated with data from 30 June 2023 from the COVID-19 Market Dashboard using the tabs 'Vaccines', 'Capacity' and filtering by 'Production locations'.[13] Once again, we are unaware of any public data sources as of 31 March and 30 April 2021.

To understand how manufacturers chose to allocate their limited initial supply of COVID-19 vaccines, we examined the number of vaccine purchases by each nation via bilateral agreements and multilateral partnerships as of 31 March 2021. As dose regimens differed by vaccine platform, we divided the total number of doses purchased by the total population of each country to establish AMCs as a percentage of population (AMC %). Data was derived from the Duke Global Health Innovation Center using the selector 'March 2021'[16] and from World Bank Total Population Statistics.[17] In addition, we examined COVID-19 vaccine price data in USD to understand if paying more led to greater vaccine security. Mean price data as of 30 June 2023 was from the COVID-19 Market Dashboard using the tabs 'Vaccines', 'Price' and filtering by 'Country/Group'.[13] Given attempts by both manufacturers and countries to closely guard prices, this source only contained data for 7 of the 10 countries in our sample. We corroborated this data with mean prices paid by HICs and LMICs as of 31 March 2022 from WHO.[21]

To quantify external vaccine distribution from manufacturer to purchaser, we divided the total vaccines delivered to each country as of 31 March 2021 by the total population of each country (Delivery %). Data was from the COVID-19 Market Dashboard using the tabs 'Vaccines', 'Delivery' and filtering by 'Month' for March 2021, and then again by 'Country'.[13] As a proxy for internal distribution, we studied the impact of the domestic public health response, as reflected by a Stringency Index as of 31 March 2021, on vaccine security. We used the Stringency Index from Our World In Data via their 'Data explorer' with the metric 'Stringency Index', the filter 'Country' and the interval '31 March 2021'.[11]

Data analysis

We used basic descriptive statistics to characterise the data obtained for each variable in our sample. To compare data between HICs and LMICs, we used basic statistics (two-sided t-tests). To explore the relationship between each supply chain predictor variable and our outcome variable of vaccine security, we used basic scatter plots. We compared at least two variables for each stage of the vaccine supply chain and used lines of best fit to visualise any relationship with vaccine security. All data analysis was conducted using Minitab V.21.4.1.

Patient and public involvement

Our study was conducted by analysing publicly available aggregate data. As such, patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

RESULTS

Vaccine security

Our analysis of vaccine security reveals wide variation between countries, with mean vaccine security at 16.3% (95% CI 1.4% to 31.2%) at the end of March and 21.7% (95% CI 5.5% to 38.0%) at the end of April. Mean vaccine security at the end of March among HICs was 29.7%, while among LMICs, it was 2.9%, resulting in a difference of 26.8% (95% CI 1.8% to 55.3%, p=0.06). Mean vaccine security at the end of April among HICs was 37.9%, while among LMICs, it was 5.6%, resulting in a difference of 32.2% (95% CI 4.2% to 60.3%, p=0.03). While the difference between HICs and LMICs improved proportionately at the end of April, the gap remained wide.

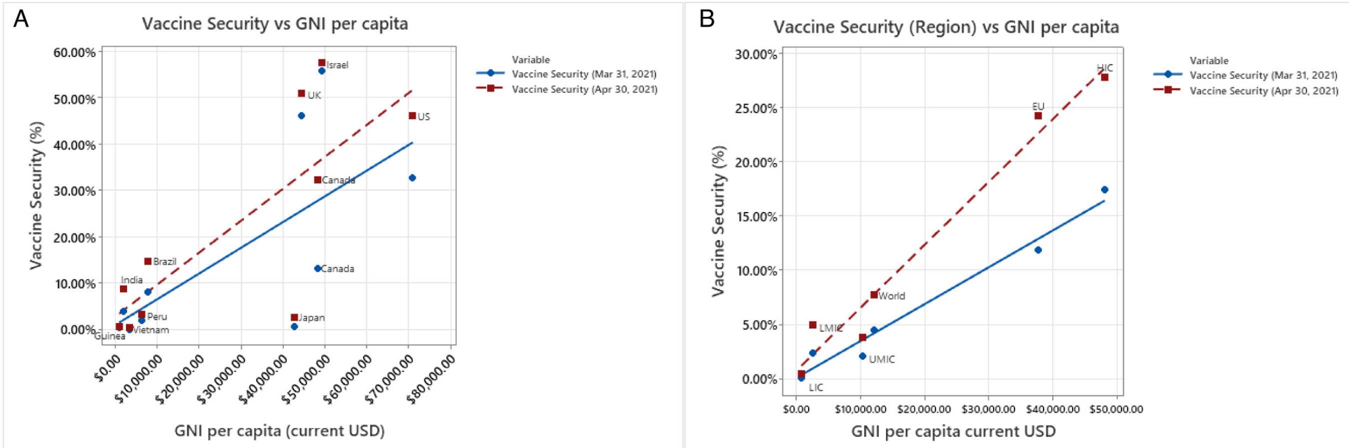

Figure 1 Relationship between vaccine security (%) and GNI per capita (A) by country and (B) by region. GNI, gross national income; USD, US dollars.

Figure 1A shows vaccine security against GNI per capita. In general, it appears that countries with greater GNI per capita had stronger vaccine security. However, we report wide variation in vaccine security among HICs, with Israel and the UK overperforming, and Canada and Japan underperforming. Interestingly, as shown in figure 1B, there appears to be an even stronger association between vaccine security and GNI per capita when data for all nations are compared categorically by income groupings.

Product

The mean number of vaccine products at all stages of development among HICs was 44.0 and among LMICs was 11.8, resulting in a difference of 32.2 (95% CI −113.2 to 48.8, p=0.33). Figure 2A shows vaccine security against

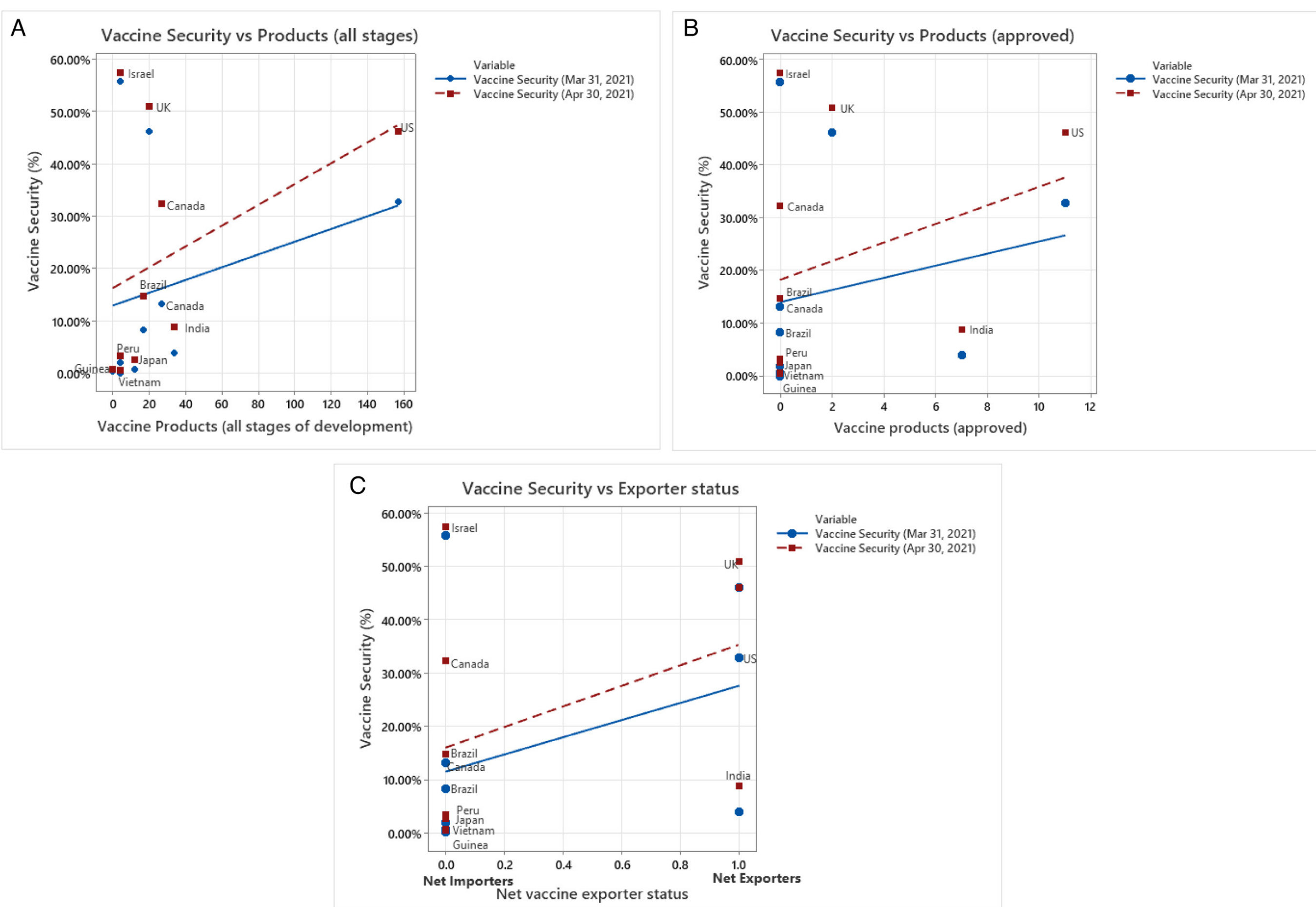

Figure 2 Relationship between vaccine security (%) and product phase variables. (A) Number of vaccine products at all stages of development. (B) Number of approved vaccine products. (C) Net vaccine exporter status.

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number of vaccine products at all stages of development. There appears to be no correlation between vaccine security and vaccine products (all stages). This lack of relationship is even more apparent when the USA is excluded from analysis. Once again, Israel and the UK overperform, and Japan underperforms relative to its HIC peers.

The mean number of vaccine products developed by HICs that received regulatory approval was 2.6, and by LMICs was 1.4, resulting in a difference of 1.2 (95% CI −7.45 to 5.05, p=0.66). Figure 2B shows vaccine security against number of vaccine products that received approval. Again, there appears to be no clear relationship between vaccine security and number of novel approved domestic vaccine products. While the USA had more vaccine products approved than any other country, Israel was able to achieve a high level of vaccine security with no domestic products that received approval.

Figure 2C shows the relationship between vaccine security and net vaccine exporter status in 2019, prior to the onset of the pandemic. Our analysis does not show a significant difference in net vaccine exporter status between HICs and LMICs (95% CI −0.95 to 0.55, p=0.55). Again, there appears to be no clear relationship between vaccine security and net vaccine exporter status. While India's overperformance on vaccine security relative to other LMICs as a net exporter stands out, we note that Israel was a net importer that still achieved a high degree of vaccine security.

Production

Figure 3A shows the relationship between vaccine security and number of COVID-19 doses produced domestically in early March 2021. Interestingly, there does not appear to be any clear correlation between vaccine security and domestic vaccine production. This lack of association is even more obvious when the USA is excluded from analysis. Furthermore, there is no significant difference in domestic vaccine production between HICs and LMICs (difference of 14522000 doses, with 95% CI −70 657 888 to 41 613 888, p=0.54).

In figure 3B, we examine the relationship between vaccine security and number of COVID-19 vaccine manufacturing facilities in each country in June 2022. Again, there appears to be no correlation between these variables. HICs had a mean of 9.4 COVID-19 manufacturing facilities and LMICs had a mean of 4.8, with no significant difference (3.6, 95% CI −20.8 to 13.5, p=0.63). This lack of association between vaccine security and the number of COVID-19 vaccine manufacturing facilities in each country was also evident in June 2023 data obtained from a different public source.[13]

Allocation

On average, the countries we studied secured AMCs to cover 265% of their population with one dose of the COVID-19 vaccine by the end of March 2021 (95% CI 89.8% to 440.2%). HICs secured significantly more doses than LMICs (difference of 336%, with 95% CI 45% to 628%, p=0.03). As shown in figure 4A, there appears to be a modest correlation between vaccine security and AMCs secured. Among HICs, Canada and Israel were significant outliers, with Canada's vaccine security lower than expected given its high AMC (%), and Israel having high vaccine security despite a modest AMC (%). In fact, if Canada were excluded from our analysis, the relationship between vaccine security and AMC (%) becomes much stronger.

Despite having access to incomplete price data, we report a very strong relationship between vaccine security and the mean price per dose paid by countries (figure 4B). As shown in figure 4C, this relationship remains strong even when data is analysed by region from a different public source.[21] HICs paid significantly more per vaccine dose than LMICs, with a mean difference of US$23.17 (95% CI, US$19.12 to US$27.22, p<0.001).

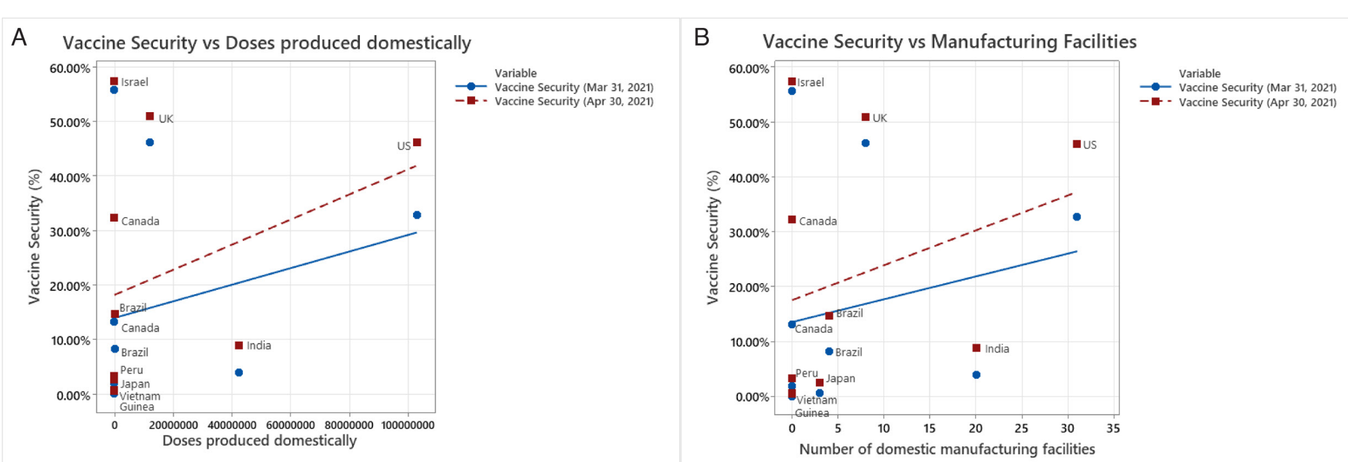

Figure 3 Relationship between vaccine security (%) and production phase variables. (A) Doses produced domestically. (B) Domestic manufacturing facilities.

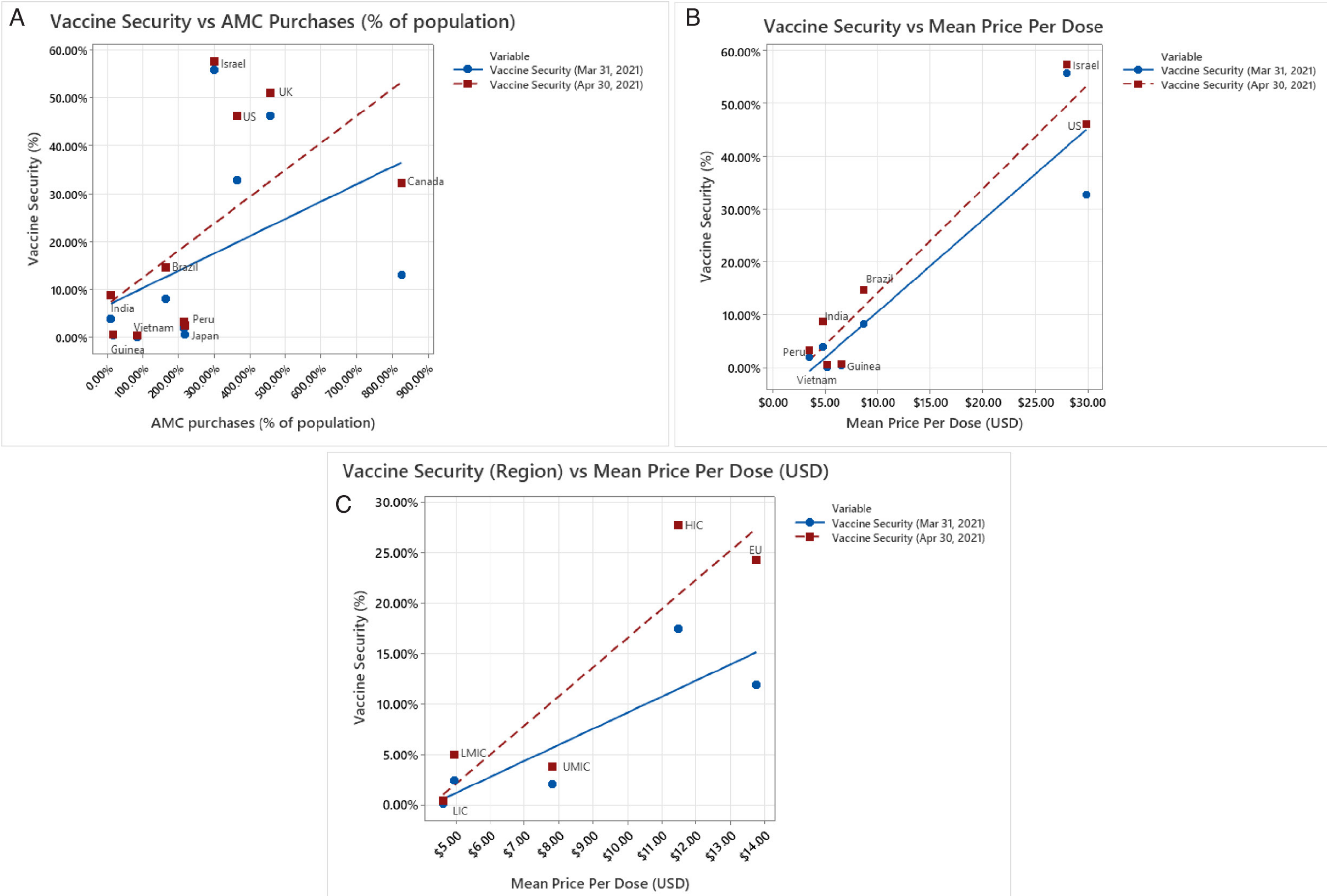

Figure 4 Relationship between vaccine security (%) and allocation phase variables. (A) AMC purchases as a percentage of population. (B) Mean Price Per Dose. (C) Mean Price Per Dose by region. AMC, advance market commitment; USD, US dollars.

Distribution

In figure 5A, we report a strong relationship between vaccine security and vaccines delivered. On average, HICs and LMICs had received deliveries to vaccinate 55.8% and 7% of their populations, respectively, by the end of March 2021, resulting in a difference of 48.8% (95% CI −118.7% to 21.1%, p=0.13).

Interestingly, as seen in figure 5B, vaccine security does not appear related to the Stringency Index at either timepoint. HICs and LMICs had a mean Stringency Index of 59.2 and 64.0, respectively, resulting in a difference of 4.75 (95% CI −10.31 to 19.81, p=0.47). There was wide intragroup heterogeneity in the public health responses

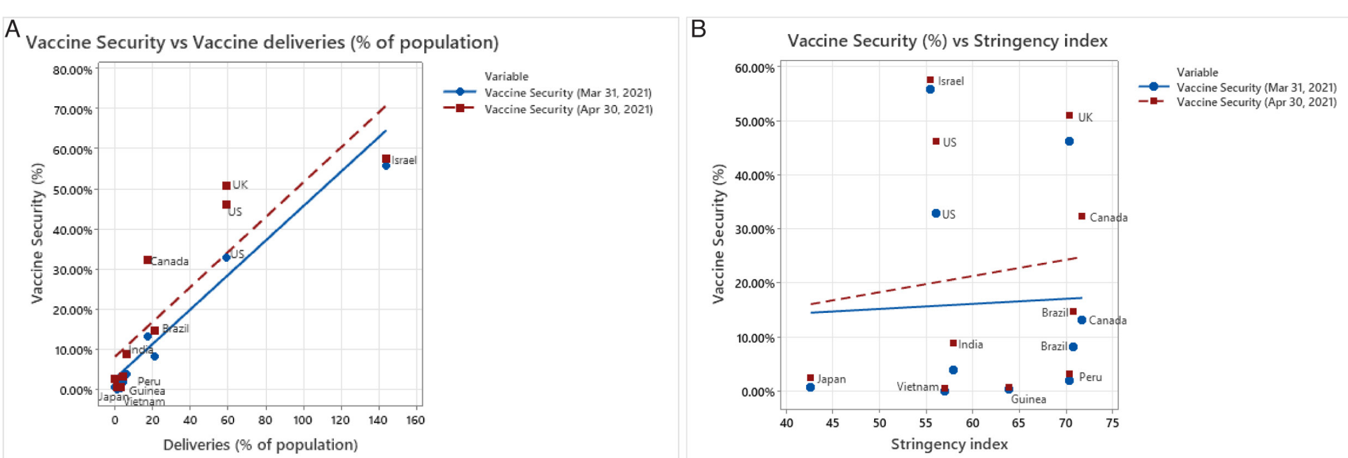

Figure 5 Relationship between vaccine security (%) and distribution phase variables. (A) Vaccine deliveries as a percentage of population. (B) Stringency Index.

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within HICs and LMICs, with Canada having the highest Stringency Index and Japan having the lowest.

Vaccine supply chain resilience refers to the ability of a vaccine supply chain to anticipate, respond to and recover from disruptions while maintaining its critical functions and ensuring high vaccine availability.[22] For the purposes of our study, high vaccine security (ie, vaccination rates) may be taken as a proxy for a highly resilient vaccine supply chain as our study focuses on the early phase of the pandemic when vaccine availability was the main Tanahashi bottleneck. Overall, our data show higher vaccine security in HICs and lower vaccine security in LMICs, with a significant difference both *between* and *within* these groupings. Our study of supply chain variables between these groups reveals a significant difference only in the allocation phase predictor variables of AMC (%) and mean price per dose. It also appears that there was large variation in supply chain resilience within HICs, with Canada, Israel and Japan being outliers on various occasions, and within LMICs, with India standing out. Our data also show a stronger relationship between vaccine security and supposedly downstream supply chain variables (vaccine purchases, price per dose and deliveries) over upstream variables (vaccine development capacity, production and manufacturing facilities). However, the presence of notable outliers in each situation suggests that one or two supply chain variables alone may be insufficient to explain all the variation in vaccine security.

DISCUSSION

The COVID-19 pandemic has highlighted the importance of vaccine security to national security. To mitigate the impact of future pandemics, the Coalition for Epidemic Preparedness Innovations envisions a future in which an effective vaccine can be developed within 100 days from the time a pathogen is sequenced or the need for a vaccine is identified.[23] As few nations can centralise, the entire vaccine supply chain within their borders, achieving this goal requires breaking down existing silos between vaccine development, manufacturing, allocation and distribution and creating global and regional frameworks for these processes to run concurrently.

In the rest of this paper, we use an OR/OM lens to reflect on observations from our country specific data. We draw four key lessons that should be of interest to policymakers who aim to strengthen vaccine security worldwide. One limitation of this study is that our underlying data may be non-parametric in nature, and there exists an inherent bias in selecting a purposive sample of countries with publicly available data. Furthermore, as only five HICs and five LMICs were sampled, our observations may not be extrapolated to all nations. A truly global picture of vaccine supply chains is also limited by the lack of reliable publicly available data on vaccination rates and domestic manufacturing capacity in China and Russia, both of which appear to have robust vaccine development programmes and were among the first to put forward vaccine candidates that received local regulatory approval. Furthermore, as each novel pathogen behaves differently, the lessons drawn from one pandemic may not be applicable to all pandemics. Last, while we focused on the early phase of the pandemic when vaccine availability was the main Tanahashi bottleneck, other factors such as vaccine acceptability (hesitancy) became increasingly important barriers as availability increased.[20]

Lesson 1: Paying more helps, but financial muscle alone cannot ensure vaccine security

Among the nations in our study, Peru paid the lowest mean price per dose. As shown in figure 1A, Peru and Brazil have similar GNI per capita. However, Brazil paid more per dose than Peru and had greater vaccine security (figure 4B). Peru also had a much smaller delivery (%) to AMC (%) ratio than Brazil (1.9% in Peru vs 12.9% in Brazil). Vaccine security in Peru was further hampered by distribution challenges, with the 'vaccine gate' scandal of February 2021 revealing that experimental COVID-19 vaccine doses were administered to influential government officials not part of the trial.[24] When Peru is compared with Brazil, it appears that a willingness to pay more per vaccine may help.

Despite having some product development capacity and securing a far higher AMC (%) than other HICs, Canada had a far lower vaccine delivery (%) compared with the US, the UK and Israel. Canada's ratio of delivery (%) to AMC (%) was only 2%, far fewer than the UK (13%), the USA (16%) and Israel (48%). Several factors may have contributed to this situation. Canada placed significant bets on vaccines that happened to enter the market late. When it eventually placed orders for mRNA vaccines, manufacturers prioritised other nations due to funding agreements and limited Canada's access to larger orders.[25] Furthermore, Canada's purchase contracts did not include advantageous delivery schedules. Last, a lack of domestic vaccine manufacturing capacity made Canada reliant on vulnerable global supply chains. Unlike other HICs that invested in infrastructure expansion, Canada's historical underfunding of vaccine manufacturing hindered its ability to produce vaccines on a large scale. This lack of capacity prevented Canada from using manufacturing contracts to control supply or accelerate deliveries.[26] Canada's experience appears to suggest that vaccine supply chains are non-linear, and a narrow focus on apparent downstream supply chain variables such as vaccine purchases, while neglecting upstream elements, may not necessarily increase vaccine security.

It has been widely reported in the literature that excess procurement by HICs can drive inequity and that any perceived benefits to HICs may be limited and short lived.[27–29] Furthermore, vaccine allocation proportional to wealth may be detrimental to all, and sharper disparities between HICs and LMICs have been shown to lead to earlier and larger outbreaks of new waves.[27]

Even after securing a far higher AMC (%) than other HICs, Canada was one of the few HICs to request doses from COVAX that were intended to build global equity.[25] Despite the above, Canada had lower vaccine security than Israel, the UK and the USA. While securing more AMCs overall appears to increase vaccine security (figure 4A), the interconnectedness of vaccine supply chain components means that financial muscle alone cannot ensure vaccine security or make up for other deficiencies.

Lesson 2: Good governance is critical to vaccine security

Our data from Israel, Japan, Brazil, Vietnam and Guinea all suggest that good governance is vital to vaccine security and may even compensate for shortcomings in certain elements of the vaccine supply chain.

Israel far outperformed its HIC peers on vaccine security, despite ranking last on product and production phase variables, and second last on AMC (%) within the HICs we studied. Nevertheless, Israel was able to secure the highest number on delivery (%). Rosen *et al* outline reasons for Israel's exceptional performance.[30] Broadly, they can be categorised into: (1) good governance (a well-established framework for swiftly addressing national emergencies), (2) strong healthcare system (a technologically coordinated system that extends to community-based providers) and (3) novel factors specific to the COVID-19 vaccine (including innovative technical solutions to address Pfizer-BioNTech vaccine's cold storage requirements and early participation in clinical trials). The Israeli experience illustrates that while preparation prior to a pandemic helps, in a time of crisis, a swift national response built on well governed public institutions and a nimble private sector may outweigh over-preparation and even make up for relative weaknesses in other elements of the vaccine supply chain.

Japan ranks 8 among the 10 countries for vaccine security, despite having novel vaccine discovery and manufacturing capacity. Japan's ratio of delivery (%) to AMC (%) was 0%, the lowest in our study. The anomalous performance of Japan is the result of a unique governance challenge—a deliberately cautious approval process by regulators due to a high level of vaccine hesitancy among the Japanese people stemming from historical safety scandals.[31] This highlights the importance of proactively working with public and private partners across all phases of the vaccine development cycle, from discovery to post-regulatory approval, to avoid unnecessary roadblocks for otherwise promising vaccine candidates.

Despite having some manufacturing capacity and having the highest vaccine security among LMICs, Brazil still lagged well behind the USA, the UK, Canada and Israel. Our AMC (%) data corroborates reports that UMICs, such as Brazil, may have exhibited greater caution in securing AMCs compared with HICs, preferring to negotiate with manufacturers only after some efficacy signals were present.[32] Furthermore, Brazil's approach to production and procurement, built on its history of domestic manufacturing and technology transfers, was slowed by regulatory hurdles and conflicts between national and state governments.[33] The case of Brazil again illustrates the importance of pandemic preparedness cooperation among public and private partners to expedite system-wide response times.

Vietnam had the lowest vaccine security in our sample, despite having a higher GNI per capita than Guinea and India. Interestingly, in 2020, with few COVID-19 cases and deaths, Vietnam was lauded for its efforts to control the spread of the virus.[34] This over-reliance on a containment approach by Vietnamese health authorities may have hampered efforts to internally distribute even delivered doses of the vaccine, as Vietnam had a vaccination rate to vaccines delivered ratio of just 5% in March 2021, the lowest among LMICs.

With no product or production stage advantages and over-reliance on the African Union's (AU) pooled purchasing power and donations, Guinea had the second lowest vaccine security in our sample. This was further complicated by political instability, with the AU suspending Guinea's membership in September 2021 after a military junta overthrew the government.[35]

Lesson 3: The presence of some domestic manufacturing capacity may provide leverage against vaccine insecurity

While domestic manufacturing capacity may not guarantee vaccine security, it appears to guard against vaccine insecurity. Despite having the second lowest GNI per capita in our study and securing the lowest AMC (%), India was second only to Brazil among LMICs when it came to vaccine deliveries and vaccine security. Possessing manufacturing capacity may have given India flexibility. Once India faced a severe second wave in April and May 2021, it enacted export restrictions to prioritise its domestic population, highlighting the importance of investing in regional manufacturing capacity in LMICs that may accelerate response times and provide a buffer against an insular global supply chain.[36]

Our data suggests that the USA excelled in the product and production phases. Despite a willingness to pay high prices, the USA did not secure as many AMCs as Canada or the UK by the end of March 2021. The American strategy appears to have focused on consolidating its upstream supply chain advantages through Operation Warp Speed to achieve large-scale vaccine manufacturing. This resulted in the production of hundreds of millions of doses by early 2021.[37] The American experience suggests that countries and transnational organisations with the means must continue to invest in and scale critical enabling competencies to further accelerate vaccine development. Despite possessing by far the greatest domestic manufacturing capacity (figure 3A), the USA did not have the highest vaccine security. In contrast to Canada, which relied too heavily on downstream elements of the supply chain, the USA appears to have counted too much on upstream variables. Despite some shortcomings, we note that the three nations with the greatest domestic manufacturing capacity (USA, India and UK) were all relatively vaccine secure compared with their peers, suggesting that having some domestic manufacturing capacity still helps. However, relying on only one or a few aspects of preparedness will not produce success.

Lesson 4: A resilient vaccine supply chain requires modest strength in multiple domains

The UK stands out in our study for its high level of vaccine security based on broad strength in all four phases of the vaccine supply chain, despite not achieving the highest scores in any one element. Baraniuk chronicles the reasons for British success, which include a focus on early novel vaccine development by Oxford University scientists that created a snowball effect, advantaging manufacturing, purchasing and delivery schedules.[38] Strengthening multiple elements of the vaccine chain may have a synergistic effect, and the redundancy created by this approach may shield against unanticipated threats posed by a novel pathogen.

CONCLUSION

Overall, our study reveals higher vaccine security in HICs and lower vaccine security in LMICs, with a significant difference both *between* and *within* these groupings. While our data show a stronger relationship between vaccine security and supposedly downstream supply chain variables (vaccine purchases, price per dose and deliveries) over upstream variables (vaccine development capacity, production and manufacturing facilities), the presence of outliers in each situation suggests that there is no silver bullet for vaccine security. Going forward, countries looking to boost vaccine security must use the COVID-19 experience to strategically strengthen deficient aspects of their supply chains, as it appears that modest strength in multiple domains may be the best approach to counteracting the effect of an unfamiliar novel pathogen.

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REFERENCES

1 World Health Organization. Vaccine security. 2022. Available: https://www.who.int/southeastasia/activities/vaccine-security#:~:text=SEARO%20%2F%20IVD-,Overview,control%20of%20severe%20infectious%20diseases [Accessed 04 Feb 2022].
2 World Health Organization. No one is safe, until everyone is safe. Available: https://www.who.int/initiatives/act-accelerator/covax [Accessed 13 Aug 2023].
3 Lancet Commission on COVID-19 Vaccines and Therapeutics Task Force Members. Operation Warp Speed: implications for global vaccine security. *Lancet Glob Health* 2021;9:e1017–21.
4 Usher AD. A beautiful idea: how COVAX has fallen short. *Lancet* 2021;397:2322–5.
5 Duijzer LE, van Jaarsveld W, Dekker R. Literature review: The vaccine supply chain. *Eur J Oper Res* 2018;268:174–92.
6 Privett N, Gonsalvez D. The top ten global health supply chain issues: Perspectives from the field. *Oper Res Health Care* 2014;3:226–30.
7 McAdams D, McDade KK, Ogbuoji O, *et al*. Incentivising wealthy nations to participate in the COVID-19 Vaccine Global Access Facility (COVAX): a game theory perspective. *BMJ Glob Health* 2020;5:e003627.
8 Van De Pas R, Widdowson M-A, Ravinetto R, *et al*. COVID-19 vaccine equity: a health systems and policy perspective. *Expert Rev Vaccines* 2022;21:25–36.
9 Zaidi A. Geographically distributed manufacturing capacity is needed for improved global health security. Bill & Melinda Gates Foundation; 2021. Available: https://www.gatesfoundation.org/ideas/articles/covid19-vaccine-geographic-distribution [Accessed 08 Jan 2024].
10 Hamadeh N, Rompaey CV, Metreau E. New world bank country classifications by income level: 2021-2022. World Bank Blogs; 2021. Available: https://blogs.worldbank.org/opendata/new-world-bank-country-classifications-income-level-2021-2022 [Accessed 05 Jan 2024].
11 Roser M, Ritchie H, Mathieu E, *et al*. Coronavirus Disease (COVID-19), Vol 1. Our World in Data, 2020. Available: https://ourworldindata.org/coronavirus
12 COVID19.trackvaccines. Vaccines – COVID19 Vaccine Tracker, Available: https://covid19.trackvaccines.org/vaccines/approved/ [Accessed 05 Jan 2024].
13 UNICEF. COVID-19 market dashboard. Available: https://www.unicef.org/supply/covid-19-market-dashboard [Accessed 13 Aug 2023].
14 World Bank. Vaccines; for human medicine exports by country in 2019. 2023. Available: https://wits.worldbank.org/trade/comtrade/en/country/ALL/year/2019/tradeflow/Exports/partner/WLD/product/300220 [Accessed 13 Aug 2023].
15 The Launch and Scale Speedometer. Vaccine purchases | launch and scale speedometer. Available: https://launchandscalefaster.org/covid-19/vaccinepurchases [Accessed 13 Aug 2023].
16 Timeline of confirmed covid vaccine purchase deals (all vaccines). Tableau; 2023. Available: https://public.tableau.com/app/profile/duke.global.health.innovation.center/viz/shared/JP8H6FRK4 [Accessed 13 Aug 2023].
17 World Bank. Population, total | data. Available: https://data.worldbank.org/indicator/SP.POP.TOTL?end=2021&start=1960 [Accessed 13 Aug 2023].
18 McCarthy N. The countries dominating Covid-19 vaccine production. Statista Infographics; 2021. Available: https://www.statista.com/chart/24492/total-covid-19-vaccine-production-by-country/ [Accessed 13 Aug 2023].

19 Global Commission for Post-Pandemic Policy. COVID-19 vaccine production, to June 30th, 2021. 2021. Available: https://globalcommissionforpostpandemicpolicy.org/covid-19-vaccine-production-to-june-30th-2021/ [Accessed 13 Aug 2023].
20 Bongers A, Riggall G, Kokareva L, *et al*. Managing the challenges associated with decreasing demand for COVID-19 vaccination in Central and West Asia. *BMJ Glob Health* 2022;7:e010066.
21 Market Information for Access to Vaccines. C-19 vaccine price data from public source and as reported by countries to WHO. 2022. Available: https://cdn.who.int/media/docs/default-source/immunization/mi4a/price-analyses-covid-vaccines-updated-period-4-2022-final.pdf?sfvrsn=b6b11a78_1&download=true [Accessed 13 Aug 2023].
22 Trump BD, Golan MS, Keisler JM, *et al*. Vaccine supply chain: Resilience-by-design and resilience-by-intervention. *Vaccine (Auckl)* 2022;40:1695–8.
23 CEPI. Delivering pandemic vaccines in 100 days. What will it take? 2022. Available: https://cepi.net/wp-content/uploads/2022/11/CEPI-100-Days-Report-Digital-Version_29-11-22.pdf?swcfpc=1 [Accessed 13 Aug 2023].
24 Perez-Brumer A, Silva-Santisteban A. The Peruvian COVID-19 vaccine scandal and re-thinking the path to public trust. *Glob Public Health* 2022;17:3119–25.
25 What is going on with Canada? Launch and Scale Speedometer; 2021. Available: https://launchandscalefaster.org/blog/what-going-canada [Accessed 13 Aug 2023].
26 Grootendorst P, Moradpour J, Schunk M, *et al*. Home remedies: how should Canada acquire vaccines for the next pandemic? Toronto CD Howe Institute; 2022. Available: https://doi.org/10.2139/ssrn.4393321
27 Ye Y, Zhang Q, Wei X, *et al*. Equitable access to COVID-19 vaccines makes a life-saving difference to all countries. *Nat Hum Behav* 2022;6:207–16.
28 Gozzi N, Chinazzi M, Dean NE, *et al*. Estimating the impact of COVID-19 vaccine inequities: a modeling study. *Nat Commun* 2023;14.
29 Moore S, Hill EM, Dyson L, *et al*. Retrospectively modeling the effects of increased global vaccine sharing on the COVID-19 pandemic. *Nat Med* 2022;28:2416–23.
30 Rosen B, Waitzberg R, Israeli A. Israel's rapid rollout of vaccinations for COVID-19. *Isr J Health Policy Res* 2021;10:6.
31 Okubo R, Yoshioka T, Ohfuji S, *et al*. COVID-19 Vaccine Hesitancy and Its Associated Factors in Japan. *Vaccines (Basel)* 2021;9:662.
32 Taylor A. The curious case of upper-middle income countries. Weekly insights and interesting trends: duke global health innovation center. 2021. Available: https://launchandscalefaster.org/blog/curious-case-upper-middle-income-countries
33 Fonseca E da, Shadlen KC, Bastos FI. The politics of COVID-19 vaccination in middle-income countries: Lessons from Brazil. *Soc Sci Med* 2021;281:114093.
34 Van Nguyen Q, Cao DA, Nghiem SH. Spread of COVID-19 and policy responses in Vietnam: An overview. *Int J Infect Dis* 2021;103:157–61.
35 Wadvalla BA. How Africa has tackled covid-19. *BMJ* 2020;370:m2830.
36 Thiagarajan K. Covid-19: India is at centre of global vaccine manufacturing, but opacity threatens public trust. *BMJ* 2021;372:196.
37 Bown CP. Covid-19 vaccine supply chains and the Defense Production Act. *Oxf Rev Econ Policy* 2022;38:771–96.
38 Baraniuk C. Covid-19: How the UK vaccine rollout delivered success, so far. *BMJ* 2021;372:421.